

**PATENT COOPERATION TREATY**  
**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
 (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PC4998JST</b>	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. <b>PCT/JP2004/012516</b>	International filing date ( <i>day/month/year</i> ) <b>31.08.2004</b>	Priority date ( <i>day/month/year</i> ) <b>27.02.2004</b>
International Patent Classification (IPC) or national classification and IPC <b>C12N15/63 (2006.01), C12N1/15 (2006.01)</b>		
Applicant <b>JAPAN SCIENCE AND TECHNOLOGY AGENCY</b>		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
a. <input checked="" type="checkbox"/> ( <i>sent to the applicant and to the International Bureau</i> ) a total of <u>2</u> sheets, as follows:
<input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
<input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
b. <input type="checkbox"/> ( <i>sent to the International Bureau only</i> ) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
<input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Faxsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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## Box No. I Basis of the report

1. With regard to the language, this report is based on:

the international application in the language in which it was filed  
 the translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:  
 international search (Rule 12.3(a) and 23.1(b))  
 publication of the international application (Rule 12.4(a))  
 international preliminary examination (Rule 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

the international application as originally filed/furnished  
 the description:  
 pages 1-28 as originally filed/furnished  
 pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 the claims:  
 nos. 2-5, 10 as originally filed/furnished  
 nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19  
 nos.\* 1, 9, 13-15 received by this Authority on 26.12.2005  
 nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 the drawings:  
 sheets fig. 1-4 as originally filed/furnished  
 sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

3.  The amendments have resulted in the cancellation of:

the description, pages \_\_\_\_\_  
 the claims, nos. 6-8, 11, 12  
 the drawings, sheets/figs \_\_\_\_\_  
 the sequence listing (*specify*): \_\_\_\_\_  
 any table(s) related to sequence listing (*specify*): \_\_\_\_\_

4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

the description, pages \_\_\_\_\_  
 the claims, nos. \_\_\_\_\_  
 the drawings, sheets/figs \_\_\_\_\_  
 the sequence listing (*specify*): \_\_\_\_\_  
 any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																									
<p>1. Statement</p> <table> <tr> <td>Novelty (N)</td> <td>Claims</td> <td><u>1-5, 9, 10, 13-15</u></td> <td>YES</td> </tr> <tr> <td></td> <td>Claims</td> <td><u></u></td> <td>NO</td> </tr> <tr> <td>Inventive step (IS)</td> <td>Claims</td> <td><u></u></td> <td>YES</td> </tr> <tr> <td></td> <td>Claims</td> <td><u>1-5, 9, 10, 13-15</u></td> <td>NO</td> </tr> <tr> <td>Industrial applicability (IA)</td> <td>Claims</td> <td><u>1-5, 9, 10, 13-15</u></td> <td>YES</td> </tr> <tr> <td></td> <td>Claims</td> <td><u></u></td> <td>NO</td> </tr> </table>			Novelty (N)	Claims	<u>1-5, 9, 10, 13-15</u>	YES		Claims	<u></u>	NO	Inventive step (IS)	Claims	<u></u>	YES		Claims	<u>1-5, 9, 10, 13-15</u>	NO	Industrial applicability (IA)	Claims	<u>1-5, 9, 10, 13-15</u>	YES		Claims	<u></u>	NO
Novelty (N)	Claims	<u>1-5, 9, 10, 13-15</u>	YES																							
	Claims	<u></u>	NO																							
Inventive step (IS)	Claims	<u></u>	YES																							
	Claims	<u>1-5, 9, 10, 13-15</u>	NO																							
Industrial applicability (IA)	Claims	<u>1-5, 9, 10, 13-15</u>	YES																							
	Claims	<u></u>	NO																							
<p>2. Citations and explanations (Rule 70.7)</p> <p>Document 1: A. J. PIERCE et al., "Ku DNA end-binding protein modulates homologous repair of double-strand breaks in mammalian cells," <i>Genes Dev.</i>, 2001, Vol. 15, No. 24, pages 3237 to 3242</p> <p>Document 2: C. ALLEN et al., "DNA dependent protein kinase suppresses double-strand break-induced and spontaneous homologous recombination," <i>Proc. Natl. Acad. Sci. USA</i>, 2002, Vol. 99, No. 6, pages 3758 to 3763</p> <p>Document 3: C. ALLEN et al., "Interactive competition between homologous recombination and nonhomologous end joining," <i>Mol. Cancer Res.</i>, 2003, Vol. 1, No. 12, pages 913 to 920</p> <p>Document 4: WO 02/52026 A2 (UNIVERSITEIT LEIDEN), 04 July 2002</p> <p>Claims 1 to 5, 9, 10 and 13 to 15  Neither the inventions set forth in claims 1 to 5, 9 and 10 nor the inventions set forth in claims 13 to 15 involve an inventive step in the light of the disclosures in newly cited documents 1 to 3, which are not cited in the international search report, and in document 4, which</p>																										

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

is cited in the international search report.

Document 1 confirms that the frequency of homologous recombination is enhanced in mammalian cells which lack the genes that are described as being necessary for heterologous recombination in the present application (e.g., KU70, XRCC4 and the like).

Meanwhile, document 2 indicates that homologous recombination is inhibited by DNA-PKcs, which is a gene that is necessary for heterologous recombination.

In addition, document 3, which was written by the author of document 2 and is cited in the reference sections of documents 1 and 2, also confirms that it is possible to enhance the frequency of homologous recombination in mammalian cells by inhibiting DNA-PKcs or the like by means of an inhibitor that is specific thereto.

Thus, the various conjectures with regard to the control mechanisms for homologous recombination and heterologous recombination have already been confirmed.

Furthermore, it is common knowledge that budding yeast is somewhat exceptional among eukaryotes. However, given the disclosures of document 4, which investigates what effects the genes that are necessary for heterologous recombination actually have upon homologous recombination in budding yeast, and the technical features that are presented in the abovementioned documents, it would have been sufficiently possible for a person skilled in the art to predict that suppressing the functions of the genes that are necessary for heterologous recombination in other filamentous eukaryotes within budding yeast will serve to impart effects similar to those described in documents 1 to 3.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
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(i.e., an enhanced homologous recombination frequency) in the budding yeast. Such being the case, the effect in question cannot be considered to be significant.

In the description of the prior art, the present application merely indicates that budding yeast is unique among eukaryotes that are not related to the inventions set forth in the present application.

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## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - on paper
    - in electronic form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in electronic form
    - furnished subsequently to this Authority for the purposes of search and/or examination
    - received by this Authority as an amendment\* on \_\_\_\_\_
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."